NIID : Neuronal Intranuclear Inclusion Disease (NIHID, INIBD : Intranuclear Inclusion Body Disease)

- Eosinophilic intranuclear inclusion in neuronal and other cells organs.
- Inclusions are ubiquitin and p62 positive and composed of filamentous materials without a limited membrane.
- Clinical manifestations are variable and antemortem diagnosis is difficult until 2011.
- The extent of neuronal loss relates to the extent of clinical manifestation.
- We reported the usefulness of skin biopsy in 2011.
- After our reports, diagnosis of adult-onset NIID cases are increasing.

Subjects

NIID except for Diagnosis. Average onset age. Average disease duration and Sex ratio, we described each value as the number for each item (Supplemental table 1, 2 and 3). We adopted 24 as the cut off score for MMSE as previous reports of incidence case/ the number of available case (%).

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Conclusion

- The number of NIID cases with dementia has increased and the morbidity rate of adult-onset NIID may be larger than previously thought.
- Almost all sporadic NIID cases present cognitive dysfunction, and 73% cases present minoris. Bladder dysfunction and ataxia rate also high.
- Head MRI detected leukoencephalopathy and DWI high intensity signal in the coritomedulary junction in most all dementia-almost dominant.
- Elevated CSF protein and abnormal nerved conduction were frequently observed, and FAB scores more obviously declined than MMSE scores.
- We must consider NIID as a differential diagnosis of leukoencephalopathy and neuropathy.
- NIID may belong to one large disease entity that presents with both dementia with leukoencephalopathy, and limb polyneuropathy.

Summary of clinical manifestations of adult onset NIID

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sporadic cases</th>
<th>Familial cases</th>
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<tbody>
<tr>
<td>Skin biopsy</td>
<td>80 (98.3%)</td>
<td>91 (81.4%)</td>
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<tr>
<td>Dementia (FAB score)</td>
<td>9 (7.7%)</td>
<td>8 (7.2%)</td>
</tr>
<tr>
<td>Limb weakness (FAB score)</td>
<td>9 (7.7%)</td>
<td>8 (7.2%)</td>
</tr>
<tr>
<td>Autopsy</td>
<td>2 (2.5%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Average onset age (range) | 63.2 (50-76) | 56.2 (43-68) |
Average disease duration (range) | 6.2 (1-19) | 7.1 (1-15) |
Sex ratio (male/female) | 14/34 | 25/30 |

Autonomic impairment | 5/10 (50%) | 4/10 (40%) |
Sensory disturbance | 10/20 (50%) | 9/18 (50%) |

Mucous weakness | 10/10 (100%) | 9/10 (90%) |

Diagnostic flowchart of adult onset NIID

| Head MRI findings of NIID
<table>
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<tbody>
<tr>
<td>Head MRI</td>
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<tr>
<td>Family 1-3</td>
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</tbody>
</table>

Evaluation of niid cases except for diagnosis. Average onset age. Average disease duration and Sex ratio, we described each value as the number for each item (Supplemental table 1, 2 and 3). We adopted 24 as the cut off score for MMSE as previous reports of incidence case/ the number of available case (%).